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Inhibin A level in the detection of preeclampsia and its severity

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Abstract

Preeclampsia (PE), a human-pregnancy-specific disease defined as the occurrence of hypertension and significant protein urea in a previously healthy woman on or after the 20th week of gestation, although its main etiology is still unknown many biochemical markers have been studded one of them is serum inhibin A. Aim of the study is to evaluate the association of maternal serum levels of inhibin A in pregnancy complicated by preeclampsia and compare it with normal non preeclamptic pregnancy and to study its usefulness in the detection of its severity. Prospective case control study of maternal human inhibin A level in pregnant women with preeclampsia in comparison with the control group in AL- Zahra Maternity Teaching Hospital. The women included in this study were divided into two groups, 50 control group who are normotensive and 50 preeclamptic patient which further divided into mild and sever. In each group cardiovascular, renal connective tissue diseases were excluded. A complete clinical history was taken from each women including; maternal age, parity, gestational age, and blood sample was taken for biochemical and hematological investigation. The blood samples were sent for liver function test, renal function test, complete blood picture and Inhibin A level. The level of inhibin A in both forms of preeclampsia, severs and mild is 154.9474±16.45767 and 150.0774±8.21035 respectively, which is significantly higher than normal control group (103.9600±14.76080). Together these data confirmed that the level of inihibin A was greater in preeclampsia than in normal pregnancy which may prove to be clinically useful laboratory markers for detection of preeclampsia.

Keywords: Preeclampsia; Pregnancy; Inhibin A

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Introduction

Preeclampsia is a unique disorder of human pregnancy with a great impact on maternal and prenatal morbidity and mortality worldwide and especially in developing countries [1]. The etiology of the condition is unknown, but placental disorders are probably involved in the pathophysiologic mechanism [2]. An increasing number of biochemical agents were evaluated as markers for predicting preeclampsia. None of them has been proved to be of clinical value yet. Much effort has been put into assessing novel potential markers and their combination with

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other screening methods such as Doppler sonography [3].

Therefore, a reliable and early placental marker could be extremely beneficial in detecting pregnant women at high-risk for preeclampsia. Recently, inhibin A, a glycoprotein mainly produced by the syncytiotrophoblast of the human placenta during pregnancy has been evaluated both for the prediction of preeclampsia [4] as well as assessment of severity [5] which can be studied easily through ELISA technique and various complications like preeclampsia, down's syndrome, aneuploidy, fetal growth restriction etc can be recognized early and further management can be planned earlier to occurrence of complications [6], and as any method to recognize the disease early can improve the prognosis this is one such study to compare the serum inhibin A levels in preeclampsia and normotensive pregnancy.

Method

Study objectives

Study the association of maternal serum levels of inhibin A in preeclamptic and non preeclamptic pregnancy

Overall study design

This study performed in Al-Zahra Maternity and Pediatrics teaching Hospital between April, 2012 and September, 2012, at this time 100 pregnant women at term pregnancy between 37-40 weeks admitted hospital were included in the study after written consent from each women after explanation the purpose of the study.

Participant, recruitment and randomization

Fifty of women had normal pregnancy and regarded as a control group and 50 of them had hypertension disorder of pregnancy at time of delivery and regarded a study group. The study group was further subdivided in to 31 patient who have mild preeclampsia (the blood pressure 140/90) and 19 of them have severe preeclampsia (when patient had blood pressure more than 160/110) [7].

At time of admission a complete clinical history was taken from each woman including maternal age, parity, gestational age, smoking, past medical history and family history of hypertensive disease and diabetes mellitus, then ask about any symptom of severe preeclampsia headache, epigastria pain and blurred vision. Exclusion of underlying renal, cardiovascular, liver and connective tissue diseases was done. Clinical examination was done to the patient including checking BP, measured in sitting position with suitable arm cuff with patient at rest using mercury sphygmomanometer using Korotokoff sound, BMI of patients calculated by weight in kg divided by height in m^2 [8], fundal height was measured and urine sample sent for albumin. The patient were considered preeclamptic when systolic and diastolic blood pressure were ≥140 /90 mmHg two consecutive reading 4-6 hours apart (the first and fifth korotekoff sounds were used in the determination of systolic and diastolic blood pressure), and ≥1+ albumin (30 mg/dl) on dipstick by qualitative estimation a random clean-

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catch urine sample (this is usually correlates with a urinalysis report of 300mg or more of protein in a timed 24-hour urine collection [9, 10].

In this study, we use the assessment of albumin in urine by dipstick. Both measured on two occasions at least 4-6 hours apart, BP was measured in 1 arm (right or left) without distinction while women were seated and after a 5-minute rest. Severe preeclampsia was considered having blood pressure ≥160/110 mmHg and protein urea at least 3+ on dip sticks [11]. None of the participant was smoker, no maternal deaths occurred, all participating women provided written informed consent prior to enrolment and the collection of blood samples after taking approval from ethical committee.

Inclusion criteria

Pregnant ladies with singleton pregnancy, and their gestational age range from 37- 40 week of gestation in labor.

The exclusion criteria include

Pregnant women with multiple pregnancies, medical diseases like chronic renal diseases, chronic hypertension, diabetes, heart disease, and obstetrical problems like multiple pregnancies were excluded from the study.

Serum samples

Five ml of peripheral venous blood (from the ante-cubital vein or from the dorsum of the hand) is drawn using a standard venipuncture techniques from each woman in the study were sent for laboratory investigations included; complete blood picture, general urine examination, blood urea, serum creatinine), serum ALT and AST, random blood sugar, and serum inhibin A.

serum inhibin A: blood samples were centrifuged for 15 minutes, sera collected and stored in deep freeze until the assay was performed in the same laboratory by ELISA (enzyme linked immune sorbent assay) and sent for liver function test, renal function test, complete blood picture and inhibin A measurement.

Reference group

A one hundred pregnant women were selected for study participation after their written consent, all of them received a detailed explanation of their condition, close follow up of them till their delivery, and women who diagnosed as having preeclampsia require close evaluation of maternal and fetal conditions for the duration of labor and even after delivery. The methods of assessment of the results done by the researcher each visit and the study was performed in accordance to Helsinki declaration and ethical approval was obtained at Kufa University in Al-Najaf city.

Statistical analysis

By using SPSS (statistical package for social sciences) version 17. We use independent sample T-test to measure the difference between two measurement data and use analysis of variance (ANOVA) to measure the difference among more than two measurement data. Setting P value <0.05 as significant.

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Results

As in (Table 1) there is no significant difference were observed in age and parity of preeclampsic group in comparison with the control group but there is significant in relationship in the systolic, diastolic blood pressure and body mass index between preeclampsia group and the control group (P-value <0.001).

Table 1
Comparison between preeclampsia and control group in different variables

Characteristic	Normal (50) mean±SD	Mild pe (31) mean±SD	Sever pe (19) mean±SD	P value
Age	25.02±5.516	26.45±6.521	28.58±6.727	0.069
Para	1.10±1.515	1.21±1.436	1.13±1.383	0.282
Systolic blood pressure mmHg	115.50±6.095	144.03±5.231	165.53±6.432	<0.001
diastolic blood pressure mmHg	70.30±5.556	94.35±4.608	107.63±8.558	<0.001
body mass index Kg/m^2	27.100±2.1783	28.681±2.138	30.332±3.9719	<0.001

Table 2
Comparison between preeclampsia and controls in different labarototy results

Characteristic	Normal (50) mean±SD	Mild pe (31) mean±SD	Sever pe (19) mean±SD	P value
SGOT IU/L	26.62±6.250	32.77±8.582	33.84±9.564	<0.001
SGPT IU/L	17.04±4.389	19.32±3.970	21.16±6.768	0.003
ALP IU/L	201.14±49.955	202.52±34.662	211.22±34.640	0.593
blood urea mg/dl	24.42±4.440	28.58±8.445	32.32±8.327	<0.001
serum creatinine mg/dl	0.7620±0.21466	0.9613±0.20925	1.0700±0.18616	<0.001
serum uric acid mg/dl	4.1170±0.93617	4.8455±1.27006	5.5879±1.08043	<0.001
TSB mg/dl	0.6560±0.20389	0.5468±0.22499	0.6189±0.23709	0.063

In (Table 2) the SGOT, SGPT, blood urea serum creatinin, and serum uric acid significantly increase in preeclampsia group in comparison with

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the control group (P-value <0.001) but there is no significant difference in the level of ALP and TSB between 2 group. There is significant increment in the inhibin A level between preeclampsia and control group but there was no significant increase of inhibin A when compared with mild and severe PE, as in the (Table 3).

Table 3
the inhibin A level between preeclampsia and control group but there was no significant increase of inhibin A

Characteristic	Normal (50)	Mild pe (31)	Sever pe (19)	P value
	mean±SD	mean±SD	mean±SD	
Inhibin A	103.9600±14.76080	150.0774±8.21035	154.9474±16.45767	<0.001

Discussion

During human pregnancy the placenta produces a variety of proteins for the establishment of the fetoplacental unit, including inhibins and activins and poor placentation in early pregnancy is thought to lead to the maternal syndrome of preeclampsia [12]. The clinical characteristics of the study population in Table 1, observed no significant difference in age and parity of preeclampsic group in comparison with the control group. As expected, there is significant in relationship in the systolic, diastolic blood pressure and body mass index between preeclampsia group & the control group (P-value <0.001). Regarding biochemical tests which shown in Table 2, the SGOT, SGPT, blood urea, serum creatinin and serum uric acid were significantly increase in preeclampsia group in comparison with the control group (P-value <0.001) but there is no significant difference in the level of ALP and TSB between 2 groups. In our study in Table 2 confirmed that the maternal serum inhibin A in PE groups were significantly higher than in controls, but there was no significant increase of inhibin A when compared with mild and severe PE, this study goes with Zongji Shenet et al [13] who found that both maternal serum and placental inhibin A in PE groups were significantly higher than in controls, but there was no severity-dependent increase of inhibin A when compared with mild and severe PE but there was no difference in inhibin A levels between PE with and without small for gestational age.

Similar study done by Shin-Young Kim et al [14] were they found that the second trimester maternal serum and amniotic fluid inhibin A levels in pregnant women who subsequently developed severe preeclampsia were significantly higher than those in normal pregnant women. Other study done by Krissada Paiwattananupant et al [15] confirms that the levels of inhibin A in the preeclampsia group

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were greater than in the normotensive group. Additional study done by Zwahlen M et al [16] found that members of the inhibin family and to some extent PAPP-A and placental growth factor are superior to other serum markers.

While Helayne M. Silver et al [17] stated that placental mRNA expression for both the α and β A subunits for both of inhibin A and activin A was increased in preeclampsia, Geralyn M. Lambert-Messerlian, et al [18] shows that second-trimester serum levels of inhibin A and hCG are modest predictors of the later onset of preeclampsia and Inhibin A may be a better predictor of early-onset preeclampsia, which is associated with a higher maternal and perinatal morbidity and mortality than preeclampsia at or near term. Nick A. Bersinger et al [19] confirm that maternal serum levels of PAPP-A, inhibin A, activin A and sE-selectin were increased in women with preeclampsia, these data also supported by Keelan et al [20] how found that in preeclampsia, activin A and inhibin A levels were markedly increased compared with controls or women with idiopathic SGA.

In Conclusion, levels of inihibin A was greater in preeclampsia than in normol pregnancy which may prove to be clinically useful laboratory markers for detection of preeclampsia.

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Competing interests

The author declares that there is no conflict of interest.

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